

## Re: Kumar A, Yadav S, Krishnappa RS, Gautam G, Raghavan N, Bakshi G, *et al.* The Urological Society of India guidelines for the evaluation and management of prostate cancer (executive summary). *Indian J Urol* 2022;38:252-7

We read with great interest and enthusiasm the publication entitled “The Urological Society of India guidelines for the evaluation and management of prostate cancer (executive summary)” in *the Indian Journal of Urology*, but were a bit disappointed with few omissions as elaborated below.<sup>[1]</sup>

In the treatment of low-risk prostate cancer, the authors have mentioned that a dose of no less than 74 Gy should be delivered either as a conventional or moderately hypofractionated radiation (HFRT) regimen (as a strong recommendation) which is misleading as the recommended dose range for conventional and hypofractionated regimens are different. Furthermore, the role of radiation therapy as a recommended treatment in intermediate-risk prostate cancer has been completely missed. Numerous randomized phase III trials of conventional fractionated radiation therapy (CFRT) have shown that doses higher than 78 Gy improve disease control (biochemical and local control) with lower salvage rates as compared to lower doses therefore doses more than 78 Gy should be recommended with CFRT in low-risk disease. Intermediate-risk and high-risk diseases should receive doses of up to 81.0 Gy.<sup>[2-6]</sup> Similarly in patients who are candidates for radiotherapy (RT), four large randomized trials have shown a clinical equipoise between moderate HFRT schedules (240 and 340 cGy per fraction) of RT and CFRT with the advantage of drastically shortening treatment durations with the use of HFRT.<sup>[7-10]</sup> It is also endorsed/preferred fractionation by modern consensus guidelines (NCCN, ASTRO, ASCO, and AUA).<sup>[11]</sup> One optimal HFRT regimen cannot be preferred over others due to lack of head-to-head comparison but commonly used schedules are 60 Gy in 20 fractions, 70 Gy in 28 fractions, 72 Gy in 30 fractions. Therefore, the dose schedule for HFRT cannot be the same as CFRT as mentioned in the guidelines.<sup>[1]</sup> Authors have completely omitted the recent encouraging evidence on the use of ultra-hypofractionated RT or stereotactic body

RT (SBRT) in low- and intermediate-risk prostate cancer. SBRT has the potential to reduce the treatment duration from 6 weeks to 5 days and is well supported by prostate radiobiology. This technology is fast catching up in India also and is being currently employed in many tertiary centers including ours since 2012.<sup>[12,13]</sup> A study of individual patient data from a cohort of 2142 patients with low- or intermediate-risk prostate cancer from 12 institutes found that the 7-year cumulative rates of biochemical recurrence (BCR) were 4.5%, 8.6%, and 14.9% for low-risk disease, favorable intermediate-risk disease, and unfavorable intermediate-risk disease, respectively with very low rate of genitourinary and gastrointestinal toxicity.<sup>[14,15]</sup> This has also been confirmed in recently published randomized studies.<sup>[16,17]</sup> The HYPO-RT-PC trial demonstrated noninferiority of 42.7 Gy in seven fractions to 78.0 Gy in 39 fractions in patients with intermediate-to-high-risk prostate cancer. Thus SBRT can also be considered as an alternative to conventionally fractionated regimens at clinics in India with appropriate technology and clinical expertise.

Under the heading of “BCR after radical prostatectomy or radiation therapy,” the authors have given a “strong recommendation” for “delayed salvage RT” after BCR which is inappropriate after the publications of three Randomized controlled trials and one high-quality meta-analysis.<sup>[18-21]</sup> The collaborative and prospectively designed systematic review and meta-analysis of the three randomized trials concludes that “early salvage RT” is the preferable treatment policy than “adjuvant RT” or “delayed salvage RT” in case of BCR.<sup>[22]</sup> This guideline has also conveniently forgotten the services rendered by brachytherapy in treating and curing millions of cancer prostate patients across all risk groups over the past 100 years.<sup>[22]</sup> In fact, interstitial brachytherapy has the same results as radical surgery or external beam RT (EBRT) in the treatment of low and intermediate prostate cancers and has level 1a evidence as boost in adjunct to EBRT for treating high-risk prostate cancers.<sup>[6,22,23]</sup> Furthermore, we believe that the statement on contraindication of brachytherapy as salvage treatment in recurrent setting needs a correction, while consensus on salvage treatment

is always difficult, brachytherapy is surely one of the few treatment options after local failure (post-RT) that is offered with radical intent.<sup>[24]</sup>

We strongly suggest re-framing the sentence as radical surgery and radical RT offers the same extent of local control and survival benefit although with different toxicity profile which needs to be discussed in detail with the patient and family before making the decision. Still, we would like to congratulate the authors, predominantly comprising of uro-surgeons (14 out of 16 authors) who scanned the evidence and published the guidelines, which we believe are somewhat incomplete as some of the relevant high-impact evidence have been overlooked. We are optimistic that this executive summary will serve as a reliable reference document after the incorporation of above-mentioned evidence and restructuring the panel by incorporating more radiation oncologists, medical oncologist, radiologist, and nuclear physician.

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